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PATHOLOGICAL STUDY OF A CASE OF MYXŒDEMA ASSOCIATED WITH TUBERCULOSIS OF THE ADRENALS:

WITH REMARKS ON THE NERVOUS SYSTEM.[1]

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The following report embodies the results of the pathological study of a typical case of myxœdema.

The disease had been gradually progressing during a period of four years, so that the dermal and neural manifestations were well marked at the time of death.

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[1] Presented, with specimens, at a meeting of the New York Society of Internal Medicine, October 19, 1904.

Especial care was devoted to the study of the nervous system, without discovering any lesion which might serve as an anatomical basis. Of unusual interest was the coexistence of an extensive chronic tuberculosis of the adrenal glands, unaccompanied by the symptoms of Addison's disease.

Summary of Case. A woman, aged fifty-one years, with well-marked nervous and cutaneous symptoms of myxœdema. Insidious onset and gradual progression. Duration four years. Death from purulent bronchitis with beginning bronchopneumonia. Autopsy: The thyroid gland was sclerosed and atrophied. The hypophysis cerebri slightly enlarged. Both suprarenal glands were the seat of extensive chronic tuberculosis. The histological examination of the central and peripheral nervous systems was entirely negative. There was well-marked generalized arteriosclerosis.

History. Admitted to Bellevue Hospital, service of Prof. Dana, April 3, 1901. The patient was a married woman, aged fifty-one years, a native of Vienna, immigrating to this country fifteen years ago. Until four years ago she had worked in a silk factory. Her parents died of old age. She has four sisters and one brother, none of whom suffered from goitre or disease similar to her own. Of four children two are living and in good health, one died the result of an accident, and one of chronic hydrocephalus. The previous history throws no light on her present trouble. She had been singularly free from any illness, this being the first time she had taken to her bed. The catamenia ceased with her forty-second year. Until then the menstruations had been regular and normal. Habits as regards alcohol, tea, and coffee were moderate, and there were no grounds for suspecting a luetic affection.

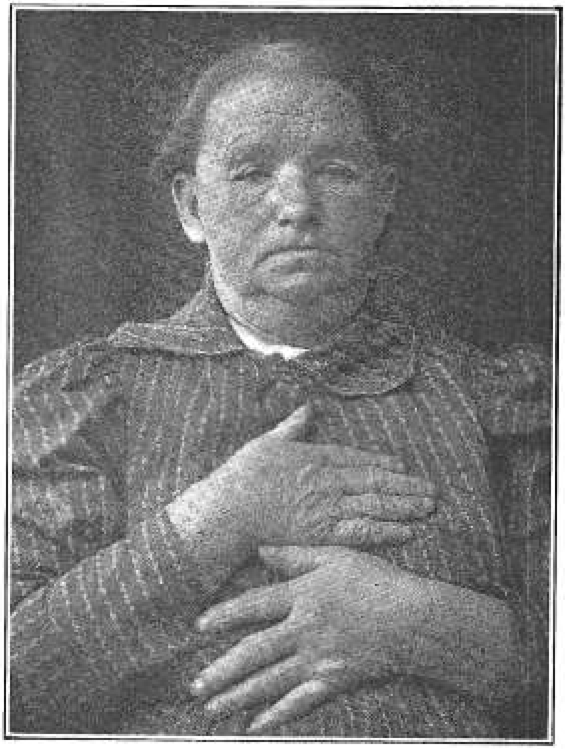
The first symptoms of the disease from which she now suffers date back four years, consisting of headaches, chiefly occipital, and vertiginous seizures. She became weak and was forced to abandon her occupation, and the hair which had never been very thick commenced to fall out. A year later the face became swollen, especially about the eyes, and persisted (Figs. 1 and 2). The legs would also swell; this, however, was inconstant and was brought on by standing and walking, disappearing in the recumbent posture. During the past three years micturition has been abnormally frequent, requiring her attention several times during the night.

The headaches continued and are growing more severe, and the vision has been failing for a year. This, with the profound weakness, brings her to the hospital.

Status Præsens. The patient is of medium height, heavily built and very corpulent. She is singularly dull and apathetic and extremely slow in thought and action.

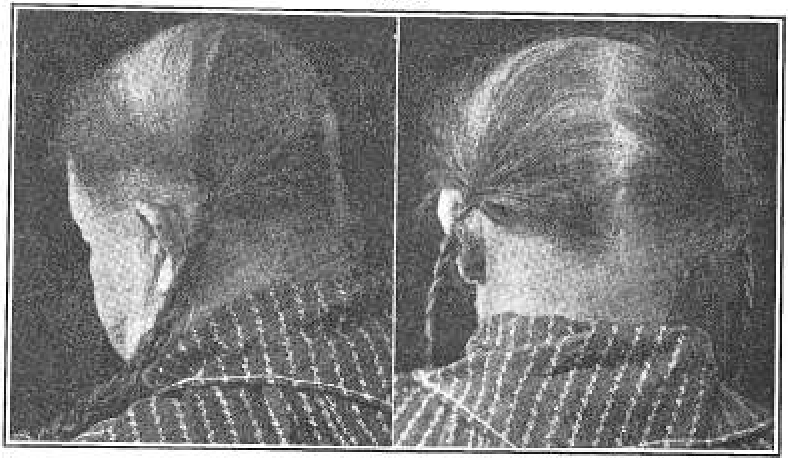
The hair of the head is coarse in texture, of a dull yellowish-brown color and very sparse. Over the top and sides of the head are areas of alopecia.

FIG. 1.



Myxœdematous deposits in the face, neck, and hands.

FIG. 2.



Loss of hair and alopecia in myxœdema.

The skin and subcutaneous tissue of the face, neck and hands are swollen and œdematous in appearance. The nose is broadened, the lips thick, the eyelids puffed and swollen, narrowing the interpalpebral fissure.

These areas of subcutaneous swelling are firm and elastic to the feel, not pitting on pressure.

The tongue is enlarged and presents a swollen appearance.

The skin of the body is dry and over the hands, forearms, feet, and legs it is quite harsh, with a tendency to scaling. The nails, with the exception of longitudinal ridging, are well preserved.

The cheeks are of a slight rosy tint, due to capillary infection and in marked contrast to the surrounding skin, which is of a yellowish, waxy hue.

The pupils are equal, responding promptly to light and accommodation.

The gross motor power, apart from great general weakness, is unimpaired.

With the exception of a blunting and a retardation there are no objective sensory disturbances.

The tendon reflexes of the lower extremities are present. Plantar flexion of the toes on stimulating the sole of the foot.

The acuity of both sight and hearing is impaired, but no gross defect is demonstrable.

The patient can stand without assistance and with the eyes closed.

The gait is extremely slow and labored, and awkward almost to inco-ordination. The slightest exertion is followed by fatigue. She complains frequently of the cold, although well clothed and in a ward of comfortable temperature.

The speech is slow and monotonous in character. Perception is very slow and a well-marked interval separates the answer and the question. The answers are, however, clear, expressing comprehension and some intelligence, but are expressed in a slow, monotonous fashion.

The memory for events of the distant past is not seriously impaired. The patient can recall with comparative ease incidents which transpired in Vienna twenty-five years ago, while happenings of recent origin have escaped her entirely.

Her mental attitude is one of apathetic complacency and torpor. She takes very little heed of her surroundings and sleeps a great deal. She is always dozing off; this happens while in conversation and at meals. Nothing seems to arouse her from this state of lethargy.

She has no hallucinations and no delusions and is neither suspicious nor irritable.

The condition of the thyroid gland cannot be determined by palpation owing to the swelling of the subcutaneous tissues at the base of the neck.

Heart. There is a moderate hypertrophy of the left ventricle with accentuation of the second aortic sound.

The pulse is full, of normal frequency, with moderate increase of the tension.

Urine. April 4, 1901: specific gravity, 1022; acid, large trace of albumin; no sugar. April 9, 1901: acid, 1013; albumin, 0.2 per cent., a few hyaline and granular casts.

Blood. Red cells, 5,112,000; white cells, 7000; hæmoglobin, 90 per cent. The differential count was normal.

Temperature. The temperature curve from April 3 to April 12 ranged between 98° and 99°. At no time was it subnormal. On April 12th the temperature rose to 101°, with the appearance of numerous rales over both lungs. Later cyanosis of the lips and finger-tips. Rapid, feeble pulse, hurried respiration. Death, April 21, 1901, eighteen days after admission.

Post-mortem Examination. The autopsy was performed by Dr. E. S. Thayer twenty-seven hours after death. Rigor mortis is well marked, muscular tissue is pale, and the subcutaneous tissue is thickened and firm. Heart is enlarged, weighs one pound, and the muscle is pale and flabby. The free borders of the mitral valve are moderately thickened, as are likewise some of the attached chordæ tendineæ.

The aortic cusps are sclerosed and in the neighborhood of their attachment adherent and thickened.

The arch of the aorta is the seat of numerous plaques of atheroma. Arteriosclerotic patches are also present in the coronary arteries. Both ventricles are hypertrophied and somewhat dilated. Beneath the pericardium a small subserous hemorrhage is visible. The pericardial sac contains 150 c.c. of clear serum.

The lungs are congested and œdematous, especially on the right side. The bronchi are filled with purulent secretion.

Adrenals. Both of the suprarenal capsules are considerably enlarged, firm and of a pale-yellow hue. The surface of section shows areas of cheesy degeneration, calcareous infiltration, with scattered islets of adrenal tissue. Kidneys are slightly enlarged. Capsule not adherent. The surface is irregular and cicatricial and contains scattered retention cysts. The cortex is swollen; markings well preserved.

Liver weighs four and one-half pounds. Surface of section dark and congested, otherwise normal.

Spleen weighs ten ounces. The capsule is thickened and adherent to surrounding parts. Surface of section congested, with moderate increase of the connective tissue.

The tongue is enlarged and the adenoid tissue at the base of the tongue and pharynx is hypertrophied.

Thyroid gland is reduced in size about one-half, is of a yellowish-white appearance and of firm sclerotic consistency. On section the surface presents but little resemblance to the normal gland. It is yellowish-white, of fibrous texture, with scarcely any sign of glandular tissue or colloid.

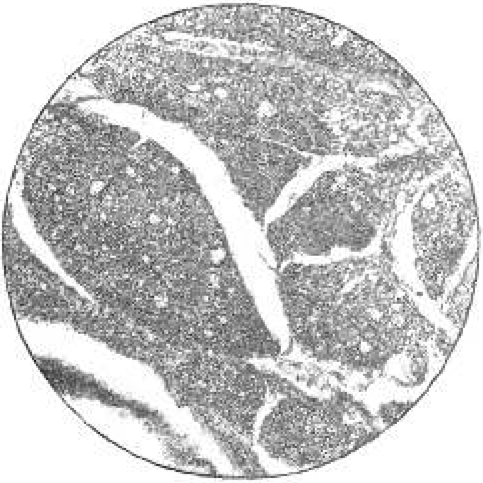
Uterus and appendages save congestion of the mucous membrane and cystic degeneration of one ovary are normal.

Brain, spinal cord, and peripheral nerves, except a moderate œdema of the cerebral pia mater and arteriosclerosis of the circle of Willis, show no gross pathological changes.

Pituitary body was slightly enlarged and hyperæmic.

Microscopic Examination. Thyroid Gland. Both lobes and the isthmus are atrophied and the seat of extensive sclerotic changes. The connective increase is greater in the peripheral portion of the gland, especially beneath the capsule, which is considerably thickened. There is scarcely any trace remaining of the normal structure of the acini with their colloidal contents. Here and there are a few miniature acini lined by flattened epithelium and containing small disks of colloid (Fig. 3).

FIG. 3.



Atrophy and sclerosis of thyroid gland. Atrophic acini containing minute disks of colloid. Hæmatoxylin and eosin.

Many of these glandular remnants are composed of dense masses of epithelial cells, broken up by connective tissue into columnar and tubular groups, and resembling fœtal thyroid structure. Some of these groups undoubtedly represent a compensatory regeneration of the glandular elements, while others are simply compressed and obliterated follicles.

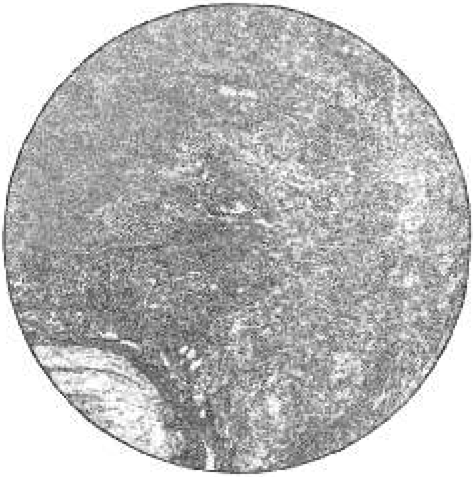
In the denser areas of the sclerosis, minute aggregations of atrophic cells are still visible, evidently the last remnant of gland structure.

Aggregations of small mononuclear round cells are also present resembling lymphoid tissue. Some of these round-cell accumulations, however, stand in immediate relation to bloodvessels, rendering it difficult to exclude a low-grade inflammatory process.

The large arteries passing into the gland while thickened, atheromatous, and containing calcareous plates are patulous throughout, as are also the larger vessels coursing within its substance.

Adrenals. The capsule of both suprarenal glands is thickened and infiltrated with round cells. The gland itself is the seat of extensive sclerotic, inflammatory and necrotic changes. Large areas of cheesy necrosis containing calcareous matter are surrounded by a dense sclerotic and inflammatory tissue containing numerous giant cells (Fig. 4).

FIG. 4.



Tuberculosis of adrenal. Round-cell infiltration. Giant cells and areas of cheesy necrosis. Hæmatoxylin and eosin.

Between and adjacent to these extensive areas of necrosis are islands of normal adrenal tissue. Approximately about one-fifth of the glandular structure of each suprarenal had been preserved. On the capsule of one of the glands is situated a small accessory suprarenal structure.

Hypophysis Cerebri. The hypophysis which to the naked eye appeared slightly enlarged, is quite normal in its histological appearances. No excess of the few globules of colloid-like material usually present in some of the acini is to be noted, and there are no evidences of glandular hypertrophy.

The bloodvessels and capillaries are distended with blood corpuscles.

Kidneys. Many of the glomeruli are sclerotic, and the capsules of others are thickened. There is some perivascular and periglomerular sclerosis fading off into the surrounding renal tissue. The arteries show a considerable degree of arteriosclerosis. The renal epithelium, except in the immediate neighborhood of the sclerotic areas, is well preserved.

Spleen. Thickening of capsule and trabeculæ. Congestion and hemorrhages.

Liver. Moderate increase of the periportal connective tissue. Congestion.

Heart Muscle. No sclerosis and no fatty degeneration. Granules of yellow pigment arranged longitudinally within the muscle fibre near the nucleus (Brown atrophy).

Pancreas. The structure is normal.

Skin. Areas examined are normal.

Tongue. Normal.

Examination of the Nervous System. The brain, spinal cord, and the anterior crural, sciatic, pneumogastric and cervical sympathetic nerves were subjected to careful study by the usual laboratory methods (Nissl, Marchi, Weigert, hæmatoxylin, eosin, and Van Gieson). The result of this examination was entirely negative.

Muscle. The muscular tissue was normal save a necrosed and sclerotic area, probably due to arteriosclerosis with vascular occlusion. In this patch there was an increase of connective tissue, round-cell infiltration, atrophy, and degeneration of the muscle fibres. The muscle spindles and intermuscular nerve fibres were normal.

REMARKS. The important and essential change consists of an extensive atrophy and sclerosis of the thyroid gland. Even those vestiges of glandular substance still remaining are compressed or undergoing atrophy.

It is important to note that the hypophysis cerebri, which normally contains disks of a colloid-like material was not the seat of any considerable compensatory hypertrophy.

The slight enlargement noted seems to be sufficiently accounted for by congestion and the normal variation in the size of this organ.

The coexistence of a chronic tuberculosis of the adrenal glands must be regarded as a rare and curious example of a pathological coincidence.

I am unable to find any record in the literature of a similar combination of lesions.

In the tables of the Report of the London Clinical Society on Myxœdema,[1] case No. 42 showed a beginning tuberculosis of the suprarenal glands. In this case, however, the tubercular manifestations were general throughout the body. In my case the characteristic symptoms of Addison's disease (pigmentation of the skin and gastrointestinal disturbances) were absent. Evidently adrenal tissue still persisted in a sufficient quantity to carry on the function of the glands.

As asthenia is common to both diseases, it is impossible to deny that this symptom was not in part due to the suprarenal changes.

Myxœdema is characterized by two groups of symptoms, the one referable to the skin and its appendages, the other to the central nervous system.

The dermal changes so characteristic of the disease are associated with the deposit of an elastic, gelatinous substance in the subcutaneous tissue yielding chemically a large proportion of mucin (50 per cent.). Halliburton, Hun and Prudden[2]).

In some cases the connective tissue surrounding the hair follicles, sebaceous and sweat glands has shown various degrees of hyperplasia.

Those symptoms indicating derangement of the central nervous organs, quite as characteristic in their way, may be grouped as general, special, and mental symptoms.

As *general* may be mentioned headaches, vertigo, insomnia, convulsions, tremor, torpor, somnolence, asthenia, motor weakness and inco-ordination, paræsthenia, and diminished sensibility.

Special. Amblyopia, limitation of the visual fields, central color scotoma, temporal hemianopia, blindness, tinnitus aurium, and deafness. Subjective sensations of taste and smell.

Mental. Loss of memory, extreme sluggishness of thought and perception, delusions, hallucinations, melancholia, and mania.

While some of these nervous manifestations may be referred with justice to the involvement of the peripheral nerve endings in the swollen skin and mucous membranes, and some to pressure on the optic chiasm by an enlarged hypophysis cerebri, the greater number are of purely central origin.

It is singular that symptoms of such gravity and persisting for so long a time, often for years, should be unattended by permanent alterations of nerve structure. But such is the case.

It has been impossible to demonstrate in the central nervous system, uniform structural change which might serve as their basis.

Those described are so inconstant, variable, and uncertain in nature, that one hesitates incorporating them in the pathology of this affection, properly speaking.

Among the lesions hitherto described may be mentioned œdema, congestion, and hemorrhages of the cerebral cortex; vacuolation and degeneration of the nerve cells, similar to those described in epilepsy (Whitewell[3]); diffuse increase of the connective tissue of the large nerve trunks; atrophy of the cerebral cortex.

Savage[4] asserts that he has observed "changes in the brain and cord which would account for progressive weak-mindedness."

In other cases the central nervous system was entirely normal.

The nervous system in the classical cases of Hun and Prudden was entirely negative.

The Sub-committee of the Clinical Society of London in their report recognized no essential changes in the cerebrospinal or sympathetic nervous systems.

The present study confirms these negative results.

Many curious theories have been advanced in the past, in explanation of the origin and mechanism of production of the nervous manifestations of myxœdema.

Hadden[5] referred the condition to a contraction of all the peripheral lymphatics, due to a disturbance of centres seated probably in the medullar and acting through the sympathetic system; even the atrophic thyroid was regarded as of secondary origin.

Clouston[6] is responsible for the ingenious theory of a saturation of the neuroglia of the brain cortex in much the same manner that the subcutaneous tissue is affected, in this way interfering with the nutrition of nerve cells and the transmission of impulses.

Others ascribed the condition to the padding of the peripheral nerve endings by the *myxœdematous* deposit, thus interfering with the transmission of afferent impulses, the central structures suffering secondarily by virtue of the defective afferent conduction.

The toxic theory is that which finds most favor at the present day, but even here authorities differ as to the exact nature of the toxic substance in question.

While all concur that the symptoms are produced by an absence of the secretion of the thyroid gland, it is still one of the mooted questions of chemical pathology as to whether this secretion is itself essential to metabolism, or whether its beneficial influence consists in neutralizing products of metabolism otherwise possessing toxic properties (Ewald[7]).

The gradual reawakening under thyroid therapy, from this state of extreme mental and physical torpor, which Charcot so aptly likened to that of hibernation in animals; the disappearance of hallucinations and delusions and the eventual complete restoration of mental and bodily health after years of partial dementia, furnish strong clinical evidence that the nerve element in myxœdema is not dependent upon organic changes in the neural structures of the body. If such are present they should rather be regarded as secondary in nature or ascribed to some other complicating factor.

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